

What is claimed is:

1. 5 DNA encoding the amino acid sequence corresponding to CTLA4Ig fusion protein reactive with B7 antigen and having ATCC No. 68629.

2. 10 A method for regulating functional CTLA4 positive T cell interactions with B7 positive cells comprising contacting said B7 positive cells with a ligand for the B7 antigen to interfere with reaction of endogenous B7 antigen with CTLA4.

3. 15 The method of claim 2, wherein said ligand is a fusion protein that contains at least a portion of the extracellular domain of CTLA4.

4. 20 The method of claim 3, wherein said ligand is CTLA4Ig fusion protein having a first amino acid sequence containing amino acid residues from about position 1 to about position 125 of the amino acid sequence corresponding to the extracellular domain of CTLA4 and a second amino acid sequence containing amino acid residues corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin C γ 1.

5. 25 30 The method of claim 3, wherein said B7 positive cells are contacted with fragments or derivatives of said CTLA4Ig fusion protein.

6. 35 The method of claim 2, wherein said ligand is a monoclonal antibody reactive with B7

antigen.

7. The method of claim 6, wherein said antibody is anti-BB1 monoclonal antibody.

5
8. The method of claim 2, wherein said B7 positive cells are B cells.

10
9. The method of claim 2, wherein the interaction of said CTLA4-positive T cells with said B7 positive cells is inhibited.

15
10. The method of claim 2, wherein said ligand is a CD28/CTLA4 Ig fusion protein hybrid having a first amino acid sequence corresponding to a portion of the extracellular domain of CD28 receptor fused to a second amino acid sequence corresponding to a portion of the extracellular domain of CTLA4 receptor and a third amino acid sequence corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin Gyl.

20
25
11. A method for regulating CTLA4-positive T cell interactions with other cells comprising inhibiting the interaction of CTLA4-positive T cells with B7 positive cells by contacting said T cells with a ligand for CTLA4.

30
30 12. The method of claim 11, wherein said ligand is B7Ig fusion protein.

35
13. The method of claim 11, wherein said ligand is a monoclonal antibody reactive with CTLA4.

14. The method of claim 13, wherein said ligand is a fragment of said monoclonal antibody.

15. 5 A method for treating immune system diseases mediated by T cell interactions with B7 positive cells comprising administering to a subject a ligand for B7 antigen, to regulate T cell interactions with said B7 positive cells.

10 16. The method of claim 15, wherein said ligand is CTLA4Ig fusion protein.

17. The method of claim 15, wherein said ligand is a CD28/CTLA4Ig fusion protein hybrid.

15 18. The method of claim 15, wherein said ligand is a monoclonal antibody reactive with B7 antigen.

20 19. The method of claim 15, wherein said T cell interactions are inhibited.

25 20. A monoclonal antibody reactive with a CTLA4Ig fusion protein having (a) a first amino acid sequence beginning with alanine at amino acid position 1 and ending with aspartic acid at amino acid position 125 (SEQ ID NO 13) of the extracellular domain of CTLA4 and (b) a second amino acid sequence containing amino acid residues of the hinge, CH2 and CH3 regions of human immunoglobulin C γ 1.

30 35 21. A monoclonal antibody reactive with the CD28/CTLA4Ig fusion protein having (a) a first amino acid sequence of a fragment of the

extracellular domain of CD28 fused to a second amino acid sequence; (b) the second amino acid sequence being a fragment of the extracellular domain of CTLA4; and (c) a third amino acid sequence containing amino acid residues of the hinge, CH₂ and CH₃ regions of human immunoglobulin Cy1.

10 22. A Chinese Hamster Ovary cell line having ATCC No. 10762 and stably expressing CTLA4Ig fusion protein.

15 23. A method for blocking B7 interaction so as to regulate the immune response comprising contacting lymphocytes with a B7-binding molecule and an IL4-binding molecule.

20 24. The method of claim 23, wherein the lymphocytes are B7 positive lymphocytes.

25 25. A method for regulating an immune response comprising contacting B7-positive lymphocytes with a B7-binding molecule and an IL4-binding molecule.

30 26. The method of claim 23 or 25, wherein the immune response is a B cell response resulting in the inhibition of antibody production.

35 27. The method of claim 23 or 25, wherein the immune response is a T cell response resulting in inhibition of cell mediated immunity.

28. The method of claim 23 or 25, wherein the immune response is an inhibition of lymphocyte

proliferation.

29. A method for inhibiting tissue transplant rejection by a subject, the subject being a recipient of transplanted tissue, which comprises administering to the subject a B7-binding molecule and an IL4-binding molecule.

30. A method for inhibiting graft versus host disease in a subject which comprises administering to the subject a B7-binding molecule and an IL4-binding molecule.

31. The method of claim 23, 25, 29, or 30, wherein the B7-binding molecule is a CTLA4Ig fusion protein.

32. The method of claim 31, wherein the CTLA4Ig fusion protein is a fusion protein having a first amino acid sequence containing amino acid residues from about position 1 to about position 125 of the amino acid sequence corresponding to the extracellular domain of CTLA4 and a second amino acid sequence containing amino acid residues corresponding to the hinge, CH₂ and CH₃ regions of human immunoglobulin Cy1.

33. The method of claim 23, 25, 29, or 30, wherein the B7-binding molecule is a CD28/CTLA4Ig fusion protein hybrid.

34. The method of claim 33, wherein the CD28/CTLA4Ig fusion protein hybrid is a fusion protein hybrid having a first amino acid

5

sequence corresponding to a portion of the extracellular domain of CD28 receptor fused to a second amino acid sequence corresponding to a portion of the extracellular domain of CTLA4 receptor and a third amino acid sequence corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin Cyl.

10

35. The method of claim 23, 25, 29, or 30, wherein the IL4-binding molecule is a monoclonal antibody which specifically recognizes and binds to IL4.

15

36. The method of claim 23, 25, 29, or 30, wherein the IL4-binding molecule is a soluble IL4 receptor which recognizes and binds to IL4.

20

37. A hybrid fusion protein reactive with B7 antigen having a first amino acid sequence corresponding to a fragment of the extracellular domain of CD28 fused to a second amino acid sequence corresponding to a fragment of the extracellular domain of CTLA4 and a third amino acid sequence corresponding to a immunoglobulin constant domain.

25

